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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/566,842	02/02/2006	Laurent Francois Andre Hennequin	056291-5233	9376
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MORGAN LEWIS & BOCKIUS LLP 1111 PENNSYLVANIA AVENUE NW WASHINGTON, DC 20004				
			EXAMINER	
			MCDOWELL, BRIAN E	
			ART UNIT	PAPER NUMBER
			1624	
			MAIL DATE	DELIVERY MODE
			11/25/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/566,842	HENNEQUIN, LAURENT FRANCOIS ANDRE	
	Examiner	Art Unit	
	BRIAN MCDOWELL	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 24 September 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 5-14 and 16 is/are pending in the application.
- 4a) Of the above claim(s) 8, 11, 13 and 16 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 5-7, 9, 10, 12, 14 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____. |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>2/2/2006, 9/24/2009</u> | 6) <input type="checkbox"/> Other: _____. |

/BEM/

DETAILED ACTION
RESPONSE TO ELECTION/RESTRICTION

Applicant's election of group I and elected specie (example 4 in specification) in the reply filed on 9/24/2009 is acknowledged. Claims 5-7, 9, 10, 12, and 14 read on the elected specie. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 8, 11, 13, and 16 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

This application contains claims drawn to an invention nonelected without traverse in the reply filed on 9/24/2009. A complete reply to this action must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

An action on the merits of claims 5-7, 9, 10, 12, and 14 is contained herein.

Priority

This application receives the foreign priority date of 8/6/2003, drawn to foreign application GB 0318422.3.

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Specification

The abstract of the disclosure is objected to because of the following. Applicant is reminded that the abstract of the disclosure should not exceed more than 150 words. Correction is required. See MPEP § 608.01(b).

Claim Objections

Claims 9 and 12 are objected to because of the following informality:

The aforementioned claims depend on claims that are withdrawn from consideration (e.g., claims 8 and 11). Correction is required.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

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Claims 5-7, 9, 10, 12, and 14 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-25 of U.S. Patent No. 7,074,800. Although the conflicting claims are not identical, they are not patentably distinct from each other because there is significant overlap between the two applications.

The genus structure seen in claim 1 of patent '800 may fully encompass the instantly claimed compounds and/or give structurally similar compounds. For instance in the instant application, compounds wherein $nc = 0$, $M = CH$, $R^{2d} = H$, $Z^a = O$, $R^{2a} = H$, and $R^{2b} = \text{-Opyrrolidinyl substituted with } C_{2-4}\text{alkanoyl}C_{1-3}\text{alkyl}$ may fall within the genus structure of claim 1 and/or give homologous compounds; thus rendering the instantly claimed compounds obvious.

Claims 5-7, 9, 10, 12, and 14 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 2-18, 20, 23, 24, and 27 of copending Application No. 11/705035. Although the conflicting claims are not identical, they are not patentably distinct from each other because there is significant overlap between the two applications.

The genus structure seen in claim 27 of application 11/705035 may fully encompass the instantly claimed compounds and/or give structurally similar compounds. For instance in the instant application, compounds wherein $nc = 0$, $M = CH$, $R^{2d} = H$, $Z^a = O$, $R^{2a} = H$, and $R^{2b} = \text{-Opyrrolidinyl substituted with } C_{2-4}\text{alkanoyl}C_{1-3}\text{alkyl}$ may fall within the genus structure of claim 27 and/or give

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homologous compounds; thus rendering the instantly claimed compounds obvious.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112 (2nd Paragraph)

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 10 and 12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 10 embraces compounds where the indole ring is attached via the oxygen atom at the *6-position*. However, there is insufficient antecedent basis for this limitation in the claim since formula IIb only embraces compounds where the indole ring is attached via an oxygen atom at the *5-position*. Claim 12 depends on claim 10 and thus is considered indefinite as it does not remedy the issues of found in claim 10.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 5-7, 9, and 10 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making and/or using pharmaceutically acceptable salts of the claimed compounds, does not reasonably provide enablement for *using* non-pharmaceutically acceptable salts of said compounds in the claimed method of use. The specification does not enable any person skilled in the art of synthetic organic chemistry to make the invention commensurate in scope with these claims. "The factors to be considered [in making an enablement rejection] have been summarized as

- a) the quantity of experimentation necessary,
- b) the amount of direction or guidance presented,
- c) the presence or absence of working examples,
- d) the nature of the invention,
- e) the state of the prior art,
- f) the relative skill of those in that art,
- g) the predictability or unpredictability of the art,
- h) and the breadth of the claims",

In re Colianni, 195 USPQ 150, *Ex parte Forman*, 230 USPQ 546. In the present case the important factors leading to a conclusion of undue experimentation are the absence of any working example, the lack of predictability in the art, and the broad scope of the claims.

- a) The instant disclosure does not teach one of ordinary skill how to administer in an efficient and practical manner non-pharmaceutically acceptable salts to a

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warm-blooded animal in need thereof for treating disease states associated with angiogenesis and/or increased vascular permeability; thus one of ordinary skill would be forced to engage in undue experimentation.

b) The specification does not provide procedural steps or parameters that would serve as direction or guidance concerning using and administering non-pharmaceutically acceptable salts to a warm-blooded animal for treating disease states associated with angiogenesis and/or increased vascular permeability.

c) There are no working examples where applicant's disclosure adequately describes how to use non-pharmaceutically acceptable salts of the instantly claimed compounds of formula IIb for treating disease states associated with angiogenesis and/or increased vascular permeability. The absence of any examples, disclosures or guidance regarding the latter is telling.

d) The instant invention relates to 4-indoloxyl substituted quinazolines of formula IIb (as well as pharmaceutically and non-pharmaceutically acceptable addition salt of said compounds) as inhibitors of VEGF for treating disease states associated with angiogenesis and/or increased vascular permeability.

f) One would have a Ph. D. degree and several years of industrial experience.

e and g) One of ordinary skill could readily search the current chemical literature and subsequently find a treasure trove of references in preparing both pharmaceutically and non-pharmaceutically acceptable addition salts of biologically active compounds. However, it is well known in the art that non-

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pharmaceutically acceptable addition salts (e.g., heavy metal and toxic salts) are not acceptable for use in a pharmaceutical setting. The aforementioned salts could not be administered to a mammal orally or intravenously without lethal consequences due to their highly toxic chemical content. Thus, the instantly claimed salts would have no application in a pharmaceutical environment. MPEP states the following:

The enablement requirement refers to the requirement of 35 U.S.C. 112, first paragraph that the specification describe how to make and how to use the invention. The invention that one skilled in the art must be enabled to make and use is that defined by the claim(s) of the particular application or patent. The purpose of the requirement that the specification describe the invention in such terms that one skilled in the art can make and use the claimed invention is to ensure that the invention is communicated to the interested public in a meaningful way.

h) The breadth of the claims include all of the hundreds of thousands of compounds of formula IIb as well as every possible addition salt (both pharmaceutically and non-pharmaceutically acceptable salts of said compounds) embraced by the claims. Thus, the scope is egregiously broad.

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue

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experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here. Thus, undue experimentation will be required to practice Applicants' invention.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BRIAN MCDOWELL whose telephone number is (571)270-5755. The examiner can normally be reached on Monday-Thursday 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson can be reached 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/B.E.M./

Patent Examiner, Art Unit 1624

/James O. Wilson/

Supervisory Patent Examiner, AU 1624